

Supplementary materials

Active constituents and mechanisms of Respiratory Detox Shot, a traditional Chinese medicine prescription, for COVID-19 control and prevention: network-molecular docking-LC-MS^E analysis

Table S1. Databases used and their detailed information.

Database Name	Version	Access date	Address	Ref
ETCM		2018	http://www.nrc.ac.cn:9090/ETCM/index.php/Home/Index/index.html	[1]
Symmap		2018	https://www.symmap.org/	[2]
NPASS	1.0	2017-10-13	http://bidd2.nus.edu.sg/NPASS/	[3]
TCMID	2.0	2017	http://119.3.41.228:8000/tcmid/	[4]
TCMSP	2.3	2014-05-31	http://www.tcmsp.com/tcmsp.php	[5]
FAF-Drugs ₄	Version 4	2017-04-26	http://fafdrugs4.mti.univ-paris-diderot.fr/index.html	[6]
Similarity ensemble approach (SEA)	Latest Version	2019-03-26	http://sea.bkslab.org/	[7]
TargetNet	1.0	2014-02-25	http://targetnet.scbdd.com/	[8]
SwissTargetPrediction		2019	http://www.swisstargetprediction.ch/index.php	[9]
UniProt		2019-10-15	https://www.uniprot.org/	[10]
GeneCards	4.13	2020-02-03	https://www.genecards.org/	[11]
String	11.0	2019-01-19	https://string-db.org/	[12]
HINT		2019-04	http://hint.yulab.org/	[13]
Cytoscape	3.7.2	2019-05-13	https://cytoscape.org/	[14]
MCODE	1.6	2020-01-15	http://apps.cytoscape.org/apps/mcode	[15]
DAVID	6.8	2016-10	https://david.ncifcrf.gov/	[16]
PDB			https://www.rcsb.org/structure/6LU7	[17]
R	3.6.1	2019-07-05	https://www.r-project.org/	[18]
Rstudio	1.2.1335	2019-04-08	https://rstudio.com/	[19]
ggplot2	3.2.1		https://ggplot2.tidyverse.org/index.html	[20]
AutoDock	4.2.6	2014-08-04	http://autodock.scripps.edu/	[21]
AutoDockVina	1.1.2	2011-05-11	http://vina.scripps.edu/	[22]
Ligplot+	2.2		https://www.ebi.ac.uk/thornton-srv/software/LigPlus/	[23]
Pymol	0.99		https://sourceforge.net/projects/pymol/files/Legacy/	[24]
ConsensusPathDB (CPDB)	Release 34	2019-01-15	http://consensuspathdb.org/	[25]
OmicSolution	26	2020-02-15	https://www.omicsolution.org/wkomics/main/	[26]

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Table S2. The number of compounds and potential targets of Respiratory Detox Shot.

TCM in RDS	Chinese name in database	Compound numbers		Target numbers
		Pre-Screening	Post- screening	
<i>Ginseng Radix et Rhizoma</i>	Renshen	190	2	78
<i>Glycyrrhizae Radix et Rhizoma</i>	Gancao	280	88	224
<i>Schizonepetiae Herba</i>	Jingjie	159	10	188
<i>Lonicerae Japonicae Flos</i>	Jinyinhua	236	17	206
<i>Armeniacae Semen Amarum</i>	Kuxingren	113	16	67
<i>Forsythiae Fructus</i>	Lianqiao	150	19	214
<i>Scrophulariae Radix</i>	Xuanshen	47	5	47
<i>Gleditsiae Spina</i>	Zaojiaoci	30	10	194
<i>Nidus Vespaee</i>	Fengfang	31	20	101

Table S3. The distribution of common compounds in TCMs of Respiratory Detox Shot.

Compound	Name	GLRR	SPH	LJF	ASA	FSF	GSRR	SR	GS	VN	SUM
MOL000211	Mairin	1	0	0	1	1	0	0	0	0	3
MOL002311	Glycyrol	1	0	0	1	0	0	0	0	0	2
MOL000359	Sitosterol	1	1	0	1	0	0	1	1	0	5
MOL000422	Kaempferol	1	0	1	0	1	1	0	1	0	5
MOL004841	Licochalcone B	1	0	0	1	0	0	0	0	0	2
MOL004903	Liquiritin	1	0	0	1	0	0	0	0	0	2
MOL004908	Glabridin	1	0	0	1	0	0	0	0	0	2
MOL005017	Phaseol	1	0	0	1	0	0	0	0	0	2
MOL000098	Quercetin	1	1	1	0	1	0	0	1	0	5
MOL000006	Luteolin	0	1	1	0	1	0	0	0	0	3
MOL000358	β -Sitosterol	0	1	1	0	1	1	1	1	0	6
MOL000449	Stigmasterol	0	1	1	1	0	0	0	1	0	4
MOL002914	Eriodictiol	0	0	1	0	0	0	0	1	0	2

ASA: *Armeniacae Semen Amarum* (Kuxingren); FSF: *Forsythiae Fructus* (Lianqiao); GLRR: *Glycyrrhizae Radix et Rhizoma* (Gancao); GS: *Gleditsiae Spina* (Zaojiaoci); GSRR: *Ginseng Radix et Rhizoma* (Renshen); LJF: *Lonicerae Japonicae Flos* (Jinyinhua); SPH: *Schizonepetiae Herba* (Jingjie); SR: *Scrophulariae Radix* (Xuanshen); VN: *Nidus Vespaee* (Fengfang).

No.	Tentative identification	Formula	MW. (D)	Observed mass		Mass error ($\times 10^{-6}$)		RT (min)	Adduct ions		Hint numbers of theoretical fragment		Source of herbs
				+	-	+	-		+	-	+	-	
83	Forsythoside C isomer	C ₂₉ H ₃₆ O ₁₆	640.1992	639.1919	-1.8	8.41			-H		4		FSF
84	6-O-Methylcatalpol	C ₁₆ H ₂₄ O ₁₀	376.1364	403.1240	-1.4	8.94			-H ₂ O+HCOO		13		LJF
85	Dinethylsecolaganoside isomer	C ₁₈ H ₂₆ O ₁₂	434.1414	433.1341	-2.4	9.09			-H		1		LJF
86	4-5-Di-O-caffeoylequinic acid methyl ester	C ₂₆ H ₂₆ O ₁₂	530.1440	529.1367	2.9	9.13			-H		0		SPH
87	Dinethylsecolaganoside isomer	C ₁₈ H ₂₆ O ₁₂	434.1419	433.1346	-1.2	9.22			-H		2		LJF
88	7- <i>epi</i> -vogeloside	C ₁₇ H ₂₄ O ₁₀	388.1365	433.1347	-0.9	9.37			+HCOO		0		LJF
89	Acteoside isomer	C ₂₉ H ₃₆ O ₁₅	624.2042	623.1969	-2.0	9.72			-H		5		FSF
90	Iososchaftoside isomer	C ₂₆ H ₂₈ O ₁₄	564.1482	609.1464	0.5	9.89			+HCOO, -H		3		FSF
91	Rutin*	C ₂₇ H ₃₀ O ₁₆	610.1537	609.1464	0.5	9.89			-H		2		VN
92	Licurazide isomer	C ₂₆ H ₃₀ O ₁₃	550.1678	549.1605	-1.5	9.95			-H		3		GLRR
93	Neoliquiritin	C ₂₁ H ₂₂ O ₉	434.1208	417.1186	-1.2	10.07			-H		4		GLRR
94	Secologanoside-7-methylester isomer	C ₁₇ H ₂₄ O ₁₂	420.1274	447.1151	1.5	10.22			-H ₂ O+HCOO		0		LJF/SPH/GS
95	3,4-Dicaffeoylquinic acid	C ₂₅ H ₂₄ O ₁₂	516.1266	515.1193	-0.4	10.68			-H		8		LJF
96	Secologanoside-7-methylester isomer	C ₁₇ H ₂₄ O ₁₂	420.1266	447.1142	-0.5	10.95			-H ₂ O+HCOO		0		LJF
97	1,3-O-dicaffeoylquinic acid isomer	C ₂₅ H ₂₄ O ₁₂	516.1266	515.1193	-0.4	10.97			-H		5		LJF
98	Matairesinoside	C ₂₆ H ₃₂ O ₁₁	520.1920	565.1902	-4.4	11.16			+HCOO		0		FSF
99	1,3-O-dicaffeoylquinic acid isomer	C ₂₅ H ₂₄ O ₁₂	516.1265	515.1192	-0.6	11.39			-H		5		LJF
100	Harpagoside_qt	C ₁₈ H ₂₀ O ₆	332.1267	359.1143	1.9	11.57			-H ₂ O, +HCOO		0		SPH
101	Liquiritin apioside	C ₂₆ H ₃₀ O ₁₃	550.1687	549.1614	0.1	11.85			-H		0		GLRR
102	(6'-O-Palmitoyl)-sitosterol-3-O- β -D-glucoside	C ₅₀ H ₈₈ O ₇	800.6563	845.6545	3.9	12.30			+HCOO		0		GSRR
103	(2S,3R,4S,5S,6R)-2-[(2S)-2-[(3S,5R,8R,9R,10R,12R,13R,14R,1 7S)-3-[(2R,3R,4S,5S,6R)-4,5- dihydroxy-6-(hydroxymethyl)-3- [(2S,3R,4S,5S,6R)-3,4,5- trihydroxy-6-(hydroxymethyl)oxan- 2-yl]oxyoxan-2-yl]oxy-12-hydroxy- 4,4,8,10,14-pentamethyl- 2,3,5,6,7,9,11,12,13,15,1	C ₄₈ H ₈₂ O ₁₈	946.5477	991.5459	-2.4	12.36			+HCOO		11		GSRR
104	ginsenoside rf isomer	C ₄₂ H ₇₂ O ₁₄	800.4901	845.4883	-2.5	12.38			+HCOO		10		GSRR
105	(2R)-7-Hydroxy-2-(4- hydroxyphenyl)chroman-4-one	C ₁₅ H ₁₂ O ₄	256.0737	255.0664	0.6	13.19			-H		0		GLRR
106	Harpagoside isomer	C ₂₄ H ₃₀ O ₁₁	494.1818	539.1800	5.6	13.59			+HCOO		0		SR
107	Sanchinoside C1	C ₄₂ H ₇₂ O ₁₄	800.4906	845.4888	-1.9	15.01			+HCOO		1		GSRR
108	Ginsenoside Rb1	C ₅₄ H ₉₂ O ₂₃	1108.6007	9	-1.9	15.67			+HCOO		5		GSRR
109	Glycyram	C ₄₂ H ₆₂ O ₁₆	822.4024	821.3951	-1.7	17.33			-H		4		GLRR
110	Glyasperins K	C ₂₂ H ₂₄ O ₅	368.1624	367.1551	0.1	19.40			-H		0		GLRR
111	Glyasperin F*	C ₂₀ H ₁₈ O ₆	354.1093	353.1021	-2.9	20.69			-H		1		GLRR
112	5,7-Dihydroxy-3-(4- methoxyphenyl)-8-(3-methylbut-2- enyl)chromone	C ₂₁ H ₂₀ O ₅	352.1334	351.1262	6.7	22.50			-H		0		GLRR/ASA/ GS
113	Licoisoflavone B*	C ₂₀ H ₁₆ O ₆	352.0941	351.0868	-1.6	22.66			-H		0		GLRR
114	Semilicoisoflavone B*	C ₂₀ H ₁₆ O ₆	352.0941	351.0868	-1.6	22.66			-H		0		GLRR
115	Licoricesaponin B2	C ₄₂ H ₆₄ O ₁₅	808.4230	853.4212	-1.7	23.71			+HCOO		0		GSRR

No.	Tentative identification	Formula	MW. (D)	Observed mass (D)		Mass error ($\times 10^{-6}$)	RT (min)	Adduct ions		Hint numbers of theoretical fragment	Source of herbs
				+	-			+	-		
116	Glyasperin C*	C ₂₁ H ₂₄ O ₅	356.1650	355.1577	7.4	27.48		-H		1	GLRR

*: The peak in the chromatogram of sample solution was validated with corresponding standard compound.

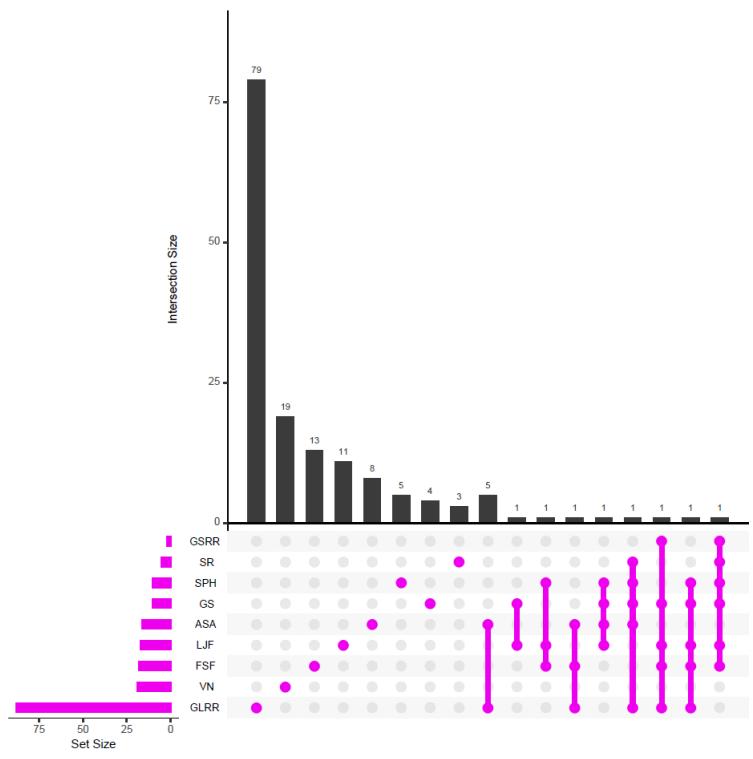


Fig. S1. Upset plot showing the number of screened compound distribution in the nine ingredients of Respiratory Detox Shot (RDS). GLRR (*Glycyrrhiza Radix et Rhizoma*) had the highest contribution to the screened compounds in RDS, followed by VN (*Nidus Vespae*) and FSF (*Forsythiae Fructus*). There were a few compounds found in more than one ingredient in the RDS prescription.

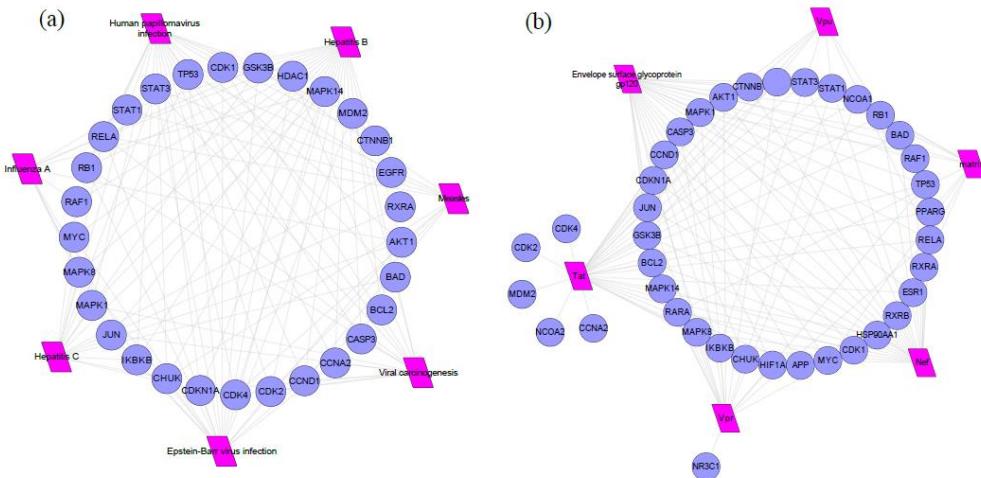


Fig. S2. The network of viral infection-related pathways in the enrichment analysis and the corresponding Respiratory Detox Shot (RDS) hub genes. a. There were 7 viral infection-related pathways enriched from 29 out of the 42 RDS hub genes, indicating the potential therapeutic effects of RDS on viral infections. Magenta, viral infection-related pathways; light purple, corresponding hub genes that are related to viral infection pathways. b. To further analyze the interaction among 42 hub genes and viral proteins, “HIV_Interaction” was applied as the background dataset from DAVID database. PPI network was constructed to demonstrate significantly dense interactions among 42 hub genes with 6 HIV proteins. Magenta, HIV proteins; light purple, corresponding hub genes that have dense interactions with HIV proteins.

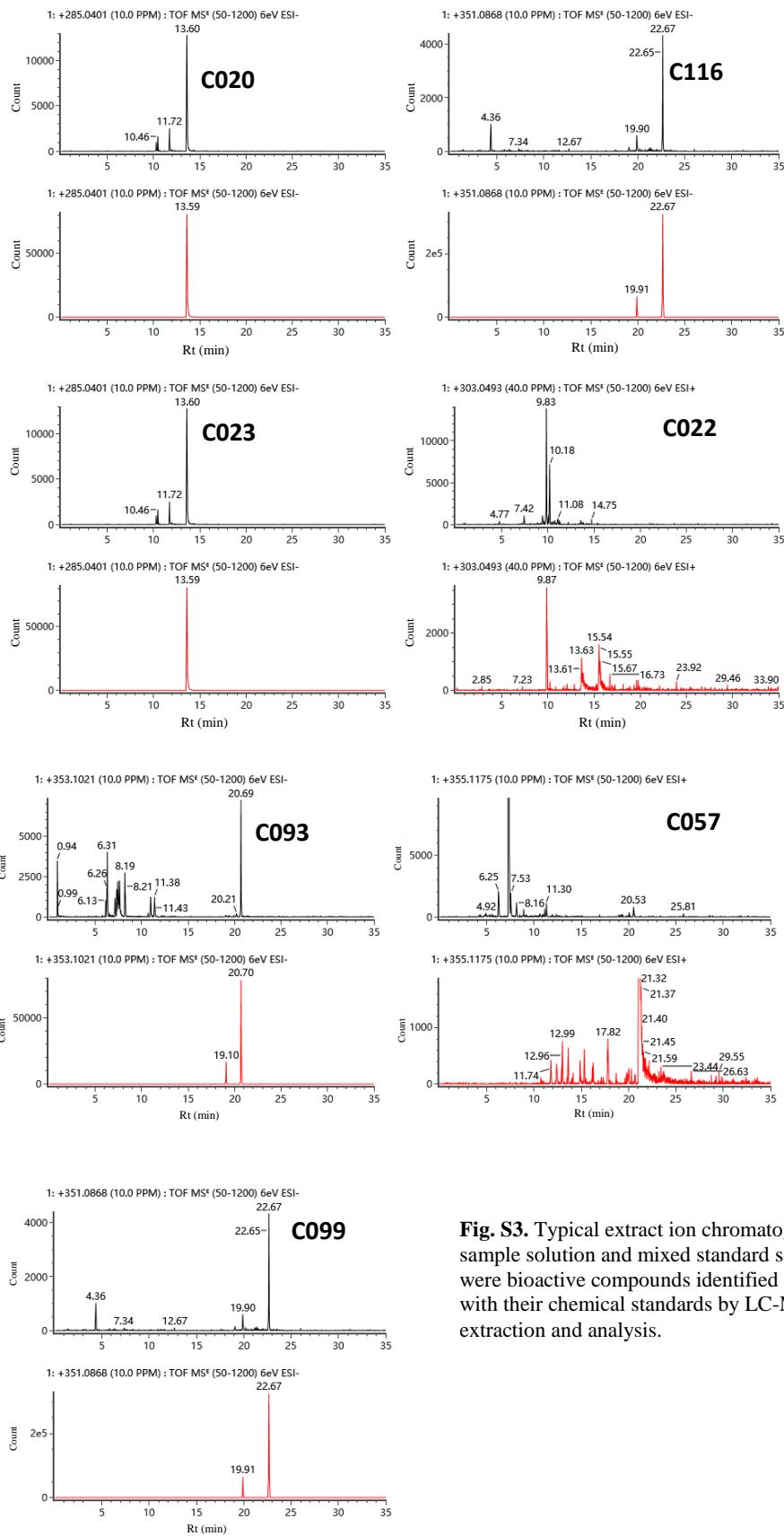


Fig. S3. Typical extract ion chromatograms of the sample solution and mixed standard solution. There were bioactive compounds identified and confirmed with their chemical standards by LC-MS^E targeted extraction and analysis.